DETAILED ACTION

Status of the Application

1. Applicant's response filed on June 23, 2009 is acknowledged. Claims 30-33 and 50-62 are currently pending. Applicant's submission of terminal disclaimers has overcome all of the previously made rejections, and therefore, they have been withdrawn. No other rejections or objections are pending.

Information Disclosure Statement

2. Applicant's submission of an Information Disclosure Statement on June 29, 2009 and on October 28, 2009 is acknowledged. Signed copies are enclosed.

It is noted that minor corrections have been made to the following non-patent literature citations appearing on the IDS filed on June 29, 2009: C1033, C1415, C1553, C1451, C1467, C1551, C1845, C1987, C2155, and C2613. Minor corrections have also been made to the following non-patent literature citations appearing on the IDS filed on October 28, 2009: C1014, C1528, C1528B, and C2402.

It is also noted that the following non-patent literature citations on the IDS filed on June 29, 2009 were not considered, because their citations do not comply with 37 CFR 1.98(b)(5): C1365, C1611, C1701, and C2385.

It is further noted that foreign patent documents B1001, B1003, and B1005 on the IDS filed on June 29, 2009 have not been considered, because a legible copy of these documents has not been provided as required by 37 CFR 1.98(a)(2).

Terminal Disclaimer

3. The terminal disclaimer filed on June 23, 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 7,312,036 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Also, the terminal disclaimer filed on June 23, 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application Serial Nos. 11/869,449, 11/331,987, 10/728,486, 11/929,910, 11/929,930, 11/930,108, 11/930,017, 11/930,002, and 11/929/707 has been reviewed and is accepted. The terminal disclaimer has been recorded.

EXAMINER'S AMENDMENT

4. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David Casimir on October 23, 2009.

In the specification:

Please amend the paragraph beginning at page 30, line 16, as follows:

The method of the present invention can also be used for detection and identification of blood-borne pathogens such as *Staphylococcus aureus* for example. The method of the present

invention can also be used for strain typing of respiratory pathogens in epidemic surveillance. Group A streptococci (GAS), or *Streptococcus pyogenes*, is one of the most consequential causes of respiratory infections because of prevalence and ability to cause disease with complications such as acute rheumatic fever and acute glomerulonephritis. GAS also causes infections of the skin (impetigo) and, in rare cases, invasive disease such as necrotizing fasciitis and toxic shock syndrome. Despite many decades of study, the underlying microbial ecology and natural selection that favors enhanced virulence and explosive GAS outbreaks is still poorly understood. The ability to detect GAS and multiple other pathogenic and non-pathogenic bacteria and viruses in patient samples would greatly facilitate our understanding of GAS epidemics. It is also essential to be able to follow the spread of virulent strains of GAS in populations and to distinguish virulent strains from less virulent or avirulent streptococci that colonize the nose and throat of asymptomatic individuals at a frequency ranging from 5-20% of the population (Bisno, A. L. (1995) in Principles and Practice of Infectious Diseases, eds. Mandell, G. L., Bennett, J. E. & Dolin, R. (Churchill Livingston, New York), Vol. 2, pp. 1786-1799). Molecular methods have been developed to type GAS based upon the sequence of the emm gene that encodes the M-protein virulence factor (Beall, B., Facklam, R. & Thompson, T. (1996) J. Clin. Micro. 34, 953-958; Beall, B., et al. (1997) J. Clin. Micro. 35, 1231-1235; Facklam, R., et al. (1999) Emerging Infectious Diseases 5, 247-253). Using this molecular classification, over 150 different emm-types are defined and correlated with phenotypic properties of thousands of GAS isolates (see the world wide web of the internet at "cdc.gov/ncidod/biotech/strep/strepindex") ~~(www.cdc.gov/ncidod/biotech/strep/strepindex.html)~~ (Facklam, R., et al. (2002) Clinical Infectious Diseases 34, 28-38). Recently, a strategy known as Multi Locus Sequence Typing

(MLST) was developed to follow the molecular Epidemiology of GAS (13). In MLST, internal fragments of seven housekeeping genes are amplified, sequenced, and compared to a database of previously studied isolates (see the world wide web of the internet at "test.mlst.net") ~~(www.test.mlst.net/)~~.

Please amend the paragraph beginning at page 32, line 22 as follows:

In other embodiments of the invention, the methods disclosed herein can be used for detection and identification of pathogens in livestock. Livestock includes, but is not limited to, cows, pigs, sheep, chickens, turkeys, goats, horses and other farm animals. For example, conditions classified by the California Department of Food and Agriculture as emergency conditions in livestock (see the world wide web of the Internet at " cdfa.ca.gov/ahfss/ah/pdfs/CA_repor- table_disease_list.sub.--05292002.pdf") ~~(www.cdfa.ca.gov/ahfss/ah/pdfs/CA_repor- table_disease_list.sub.--05292002.pdf)~~ include, but are not limited to: Anthrax (*Bacillus anthracis*), Screwworm myiasis (*Cochliomyia hominivorax* or *Chrysomya bezziana*), African trypanosomiasis (Tsetse fly diseases), Bovine babesiosis (*piroplasmosis*), Bovine spongiform encephalopathy (Mad Cow), Contagious bovine pleuropneumonia (*Mycoplasma mycoides mycoides* small colony), Foot-and-mouth disease (Hoof-and-mouth), Heartwater (*Cowdria ruminantium*), Hemorrhagic septicemia (*Pasteurella multocida* serotypes B:2 or E:2), Lumpy skin disease, Malignant catarrhal fever (African type), Rift Valley fever, Rinderpest (Cattle plague), Theileriosis (Corridor disease, East Coast fever), Vesicular stomatitis, Contagious agalactia (*Mycoplasma species*), Contagious caprine pleuropneumonia (*Mycoplasma capricolum capripneumoniae*), Nairobi sheep disease, Peste des

petits ruminants (Goat plague), Pulmonary adenomatosis (Viral neoplastic pneumonia), *Salmonella abortus ovis*, Sheep and goat pox, African swine fever, Classical swine fever (Hog cholera), Japanese encephalitis, Nipah virus, Swine vesicular disease, Teschen disease (*Enterovirus encephalomyelitis*), Vesicular exanthema, Exotic Newcastle disease (Viscerotropic velogenic Newcastle disease), Highly pathogenic avian influenza (Fowl plague), African horse sickness, Dourine (*Trypanosoma equiperdum*), Epizootic lymphangitis (equine blastomycosis, equine histoplasmosis), Equine piroplasmosis (*Babesia equi, B. caballi*), Glanders (Farcy) (*Pseudomonas mallei*), Hendra virus (*Equine morbillivirus*), Horse pox, Surra (*Trypanosoma evansi*), Venezuelan equine encephalomyelitis, West Nile Virus, Chronic wasting disease in cervids, and Viral hemorrhagic disease of rabbits (calicivirus).

Please amend the paragraph beginning at page 57, line 2 as follows:

Emm-typing primers: The allelic profile of a GAS strain by Multilocus Sequencing Technique (MLST) can be obtained by sequencing the internal fragments of seven housekeeping genes. The nucleotide sequences for each of these housekeeping genes, for 212 isolates of GAS (78 distinct emm types), are available (on the world wide web of the Internet at "mlst.net") ~~(www.mlst.net)~~. This corresponds to one hundred different allelic profiles or unique sequence types, referred to by Enright et al. as ST1-ST100(Enright, M. C., et al., Infection and Immunity 2001, 69, 2416-2427). For each sequence type, we created a virtual transcript by concatenating sequences appropriate to their allelic profile from each of the seven genes. MLST primers were designed using these sequences and were constrained to be within each gene loci. Twenty-four primer pairs were initially designed and tested against the sequenced GAS strain 700294. A final

subset of six primer pairs Table 11 was chosen based on a theoretical calculation of minimal number of primer pairs that maximized resolution of between emm types.

Please amend the paragraph beginning at page 58, line 1 as follows:

Bacterial genomic DNA samples of all isolates were extracted from freshly grown GAS strains by using QIAamp DNA Blood Mini Kit (Qiagen, Valencia, Calif.) according to the procedures described by the manufacture. Group A streptococcal cells were subjected to PCR and sequence analysis using emm-gene specific PCR as previously described (Beall, B., et al. J. Clin. Micro., 1996, 34, 953-958; Facklam, R., et al. Emerg. Infect. Dis. 1999, 5, 247-253). Homology searches on DNA sequences were conducted against known emm sequences present in (on the world wide web of the Internet at "cdc.gov/ncidod/biotech/infotech_hp") ~~(www.cdc.gov/ncidod/biotech/infotech_hp.html)~~. For MLST analysis, internal fragments of seven housekeeping genes, were amplified by PCR and analyzed as previously described (Enright, M. C., et al., Infection and Immunity 2001, 69, 2416-2427). The emm-type was determined from comparison to the MLST database.

Reasons for Allowance

5. The following is an examiner's statement of reasons for allowance: The instant claims are drawn to a method for identifying a virus in a sample using PCR amplification and mass spectroscopy. The method requires the use of a pair of amplification primers that flanks a variable region and comparison of the base composition obtained by analysis of the amplification products by mass spectroscopy to those found in a database comprising five or more known base

compositions. There is no prior art that anticipates the claimed method. The declaration filed on October 6, 2006 overcomes the *prima facie* case of obviousness cited in the prior Office Action. As noted in related cases, the skepticism in the art evidenced by the Buchsbaum declaration is persuasive as a secondary consideration of non-obviousness. The skepticism of the JASON group in an internal review and the conclusion that the project was unlikely to be successful (point 3 of the declaration) persuasively argues that the claimed invention is not obvious.

It is further noted that the references and cited combination of art in the Information Disclosure Statement filed on June 29, 2009 have been fully reviewed and considered, but they were not found to be relevant to allowability of the instant claims based on the evidence made of record by the Declaration filed on October 6, 2006. Accordingly, the claimed invention is deemed novel and unobvious.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/GARY BENZION/
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